Propagation of Errors from Nuisance Parameters in qMRI

Mark D. Does, PhD
Vanderbilt University

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Propagation of Error From Parameter Constraints in Quantitative MRI: Example Application of Multiple Spin Echo T_2 Mapping

Christopher L. Lankford[1,2] and Mark D. Does[1,2,3,4]*

Quantitative MRI (qMRI): Overview

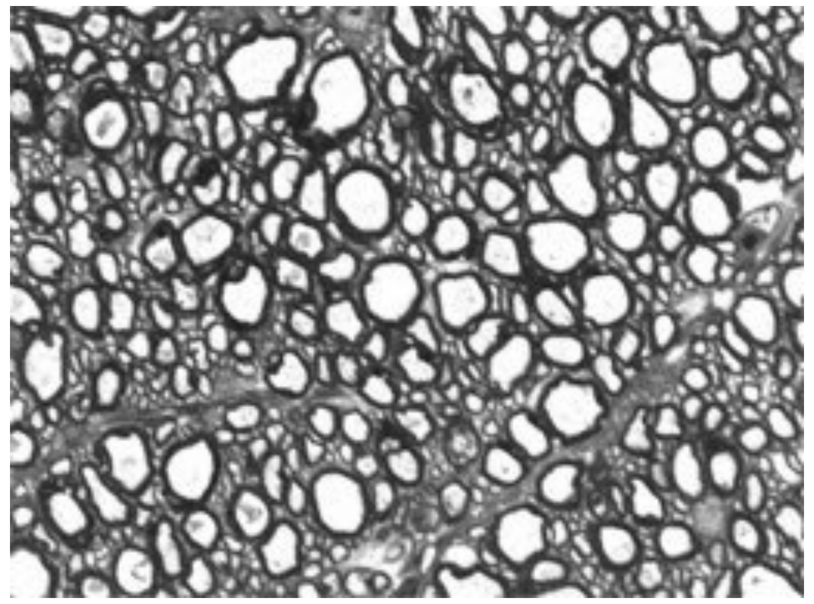
- Provide quantitative measures that are suitably:
  - Accurate
  - Precise
  - Efficient
  - Robust
  - Useful

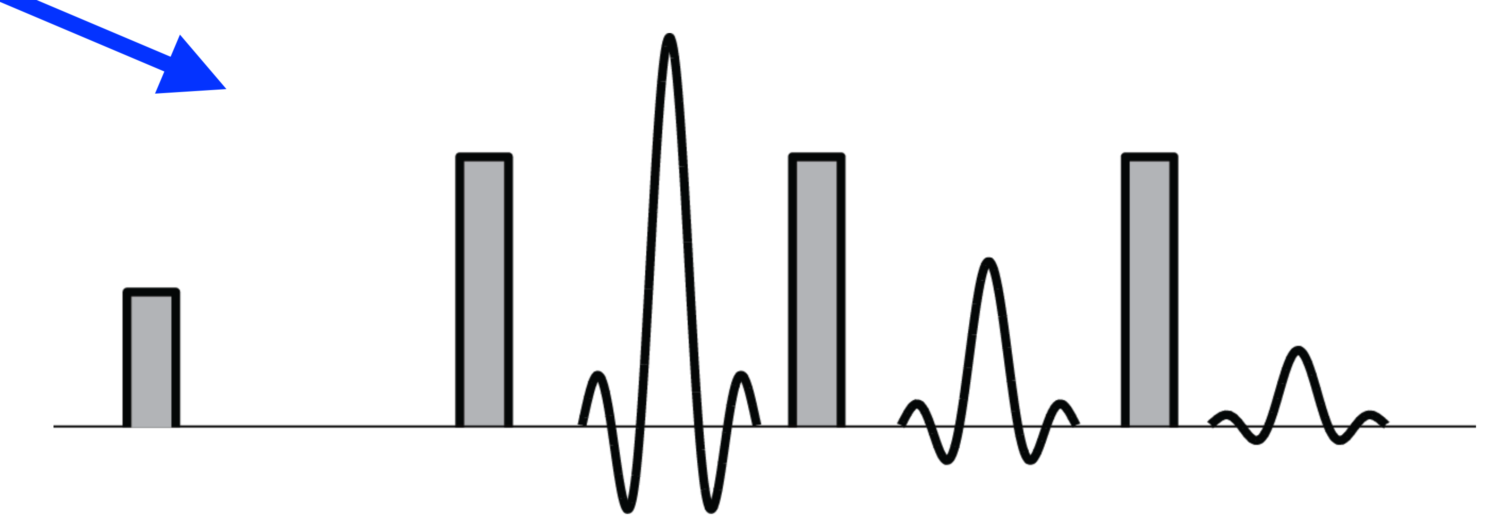
qMRI: Overview

$\beta_1, \beta_2, \ldots$ $\ldots \beta_{M-1}, \beta_M$

Tissue/Signal Modeling

Sequence Design





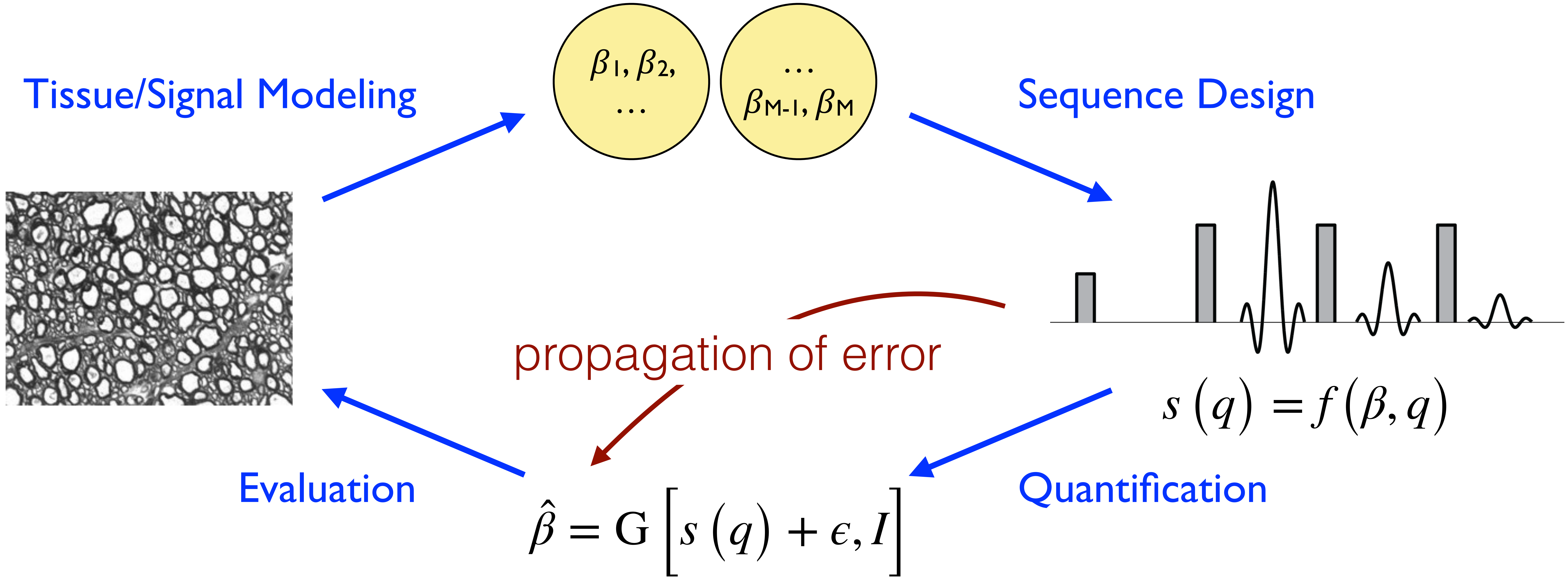
$$s(q) = f(\beta, q)$$

Evaluation

Quantification

$$\hat{\beta} = \mathrm{G}\left[s(q) + \epsilon, I\right]$$

qMRI: Overview



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- The signal is a function of parameters,

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  - independent parameters, known
    e.g., T_E, T_R, …
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    - parameters of interest
      e.g., M_0, T_2, T_1, …
      - freely fitted, β_{f}

$$s\left(q\right) = f\left(\beta, q\right)$$

independent parameters

model parameters

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  - model parameters, <u>unknown</u>
    - parameters of interest
      e.g., M_0, T_2, T_1, …
      - freely fitted, β_f
    - nuisance parameters
      e.g,. B_1, B_0, …
      - may be constrained, β_c
        or fitted, β_f

$$s\left(q\right) = f\left(\beta, q\right)$$

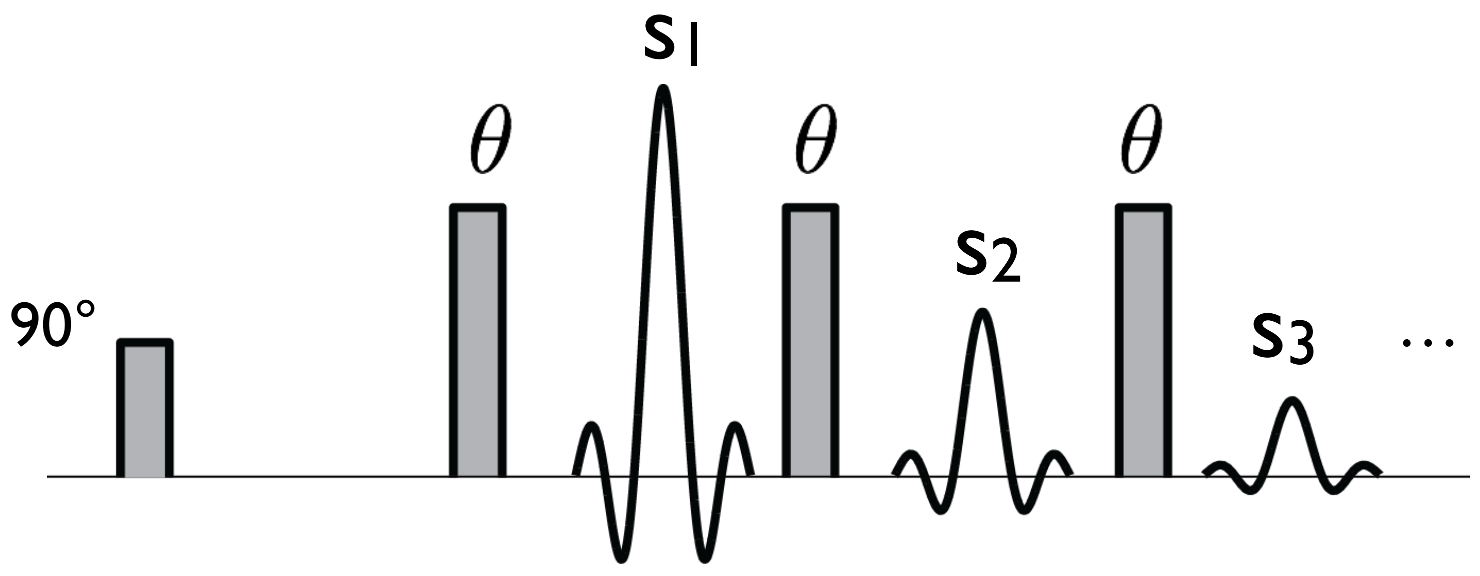
independent parameters

model parameters

$$\beta = \begin{bmatrix} \beta_\mathrm{f} \\ \beta_\mathrm{c} \end{bmatrix}$$

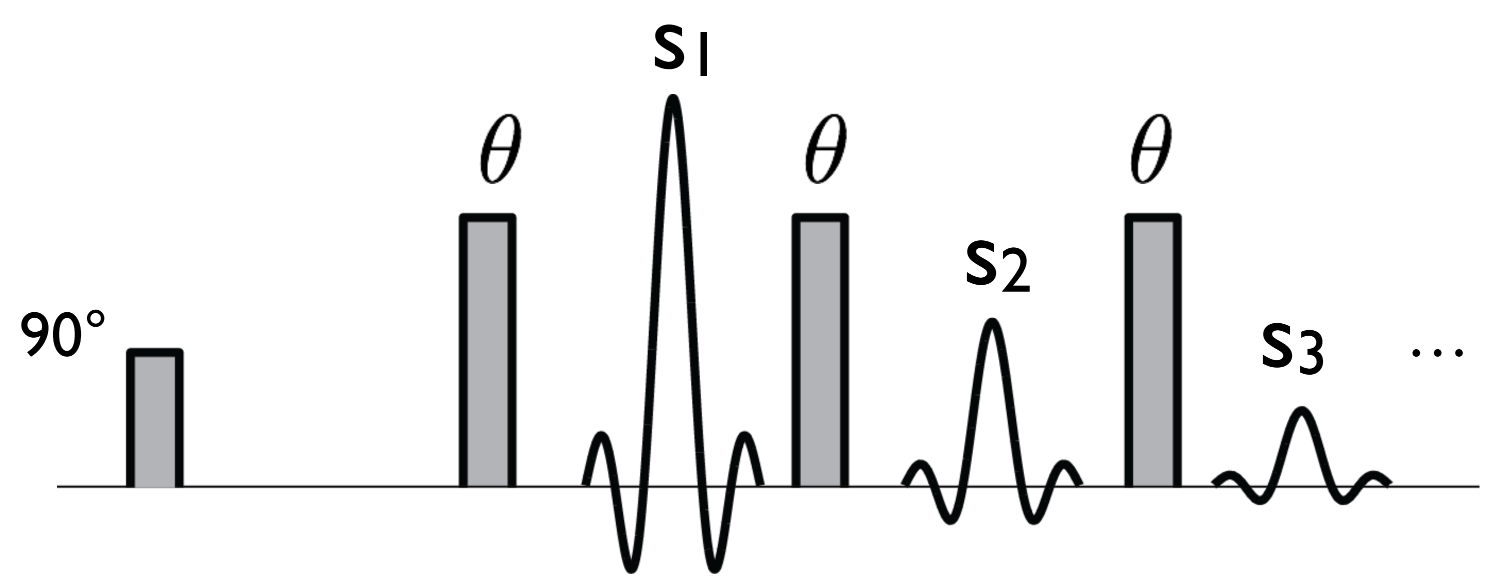
E.g., T_2 Measurement

- Objective: measure T_2 via multiple spin echo MRI



E.g., T_2 Measurement

- Objective: measure T_2 via multiple spin echo MRI
- Signal Equation, $s\left(t_e\right) = \mathrm{EPG}\left[t_e; M_0, T_2, \theta\right]$
- Model parameters of interest: M_0, T_2
- Nuisance parameter: θ



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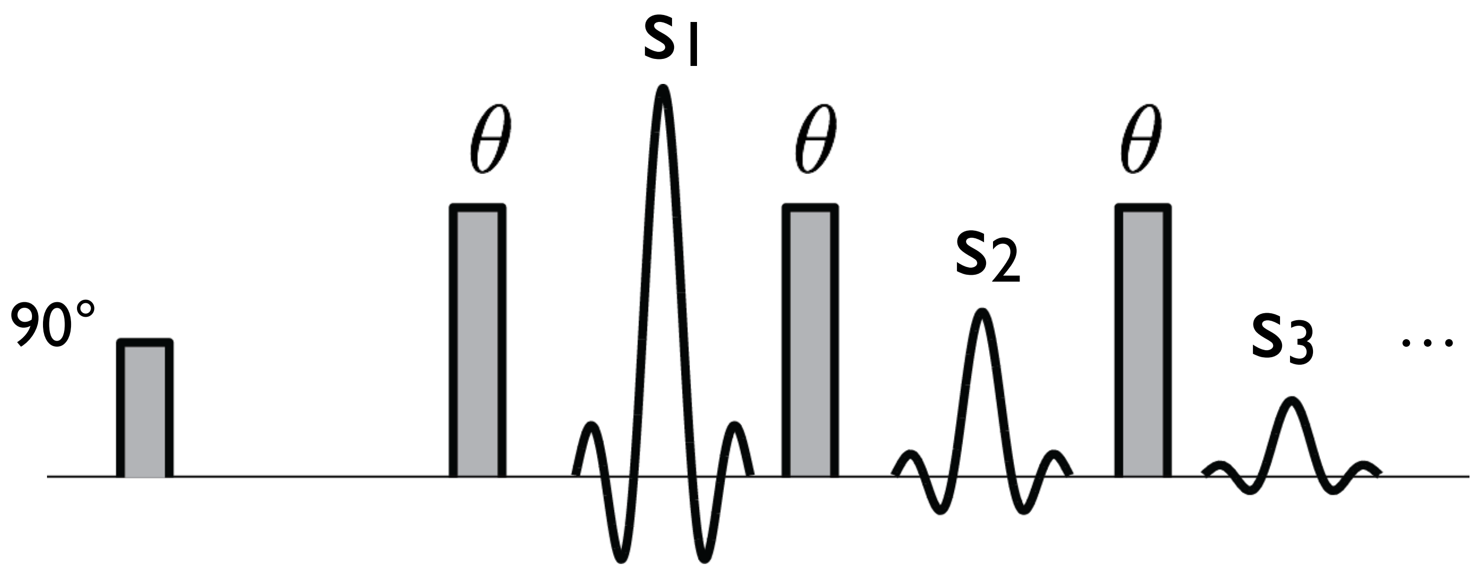

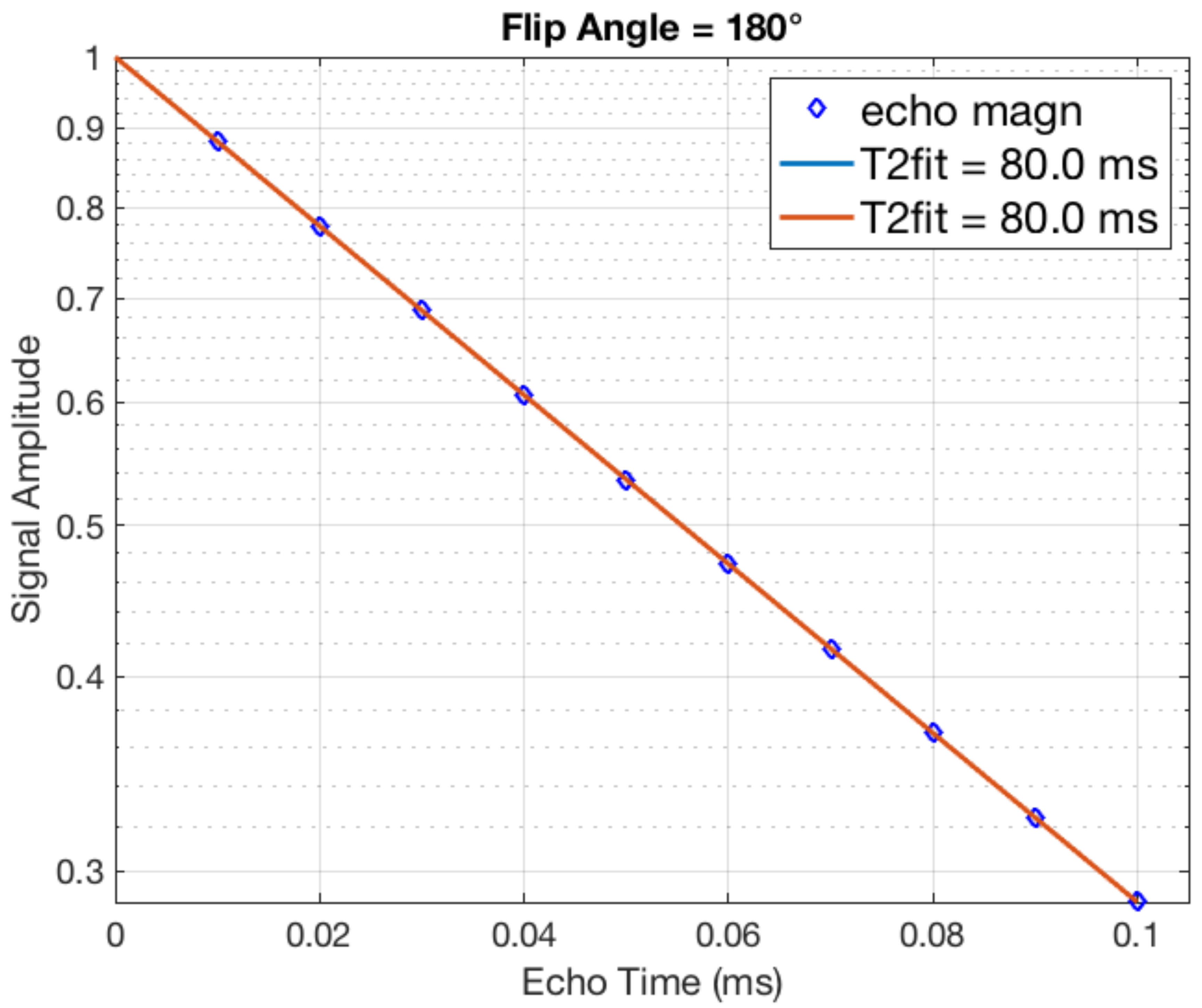

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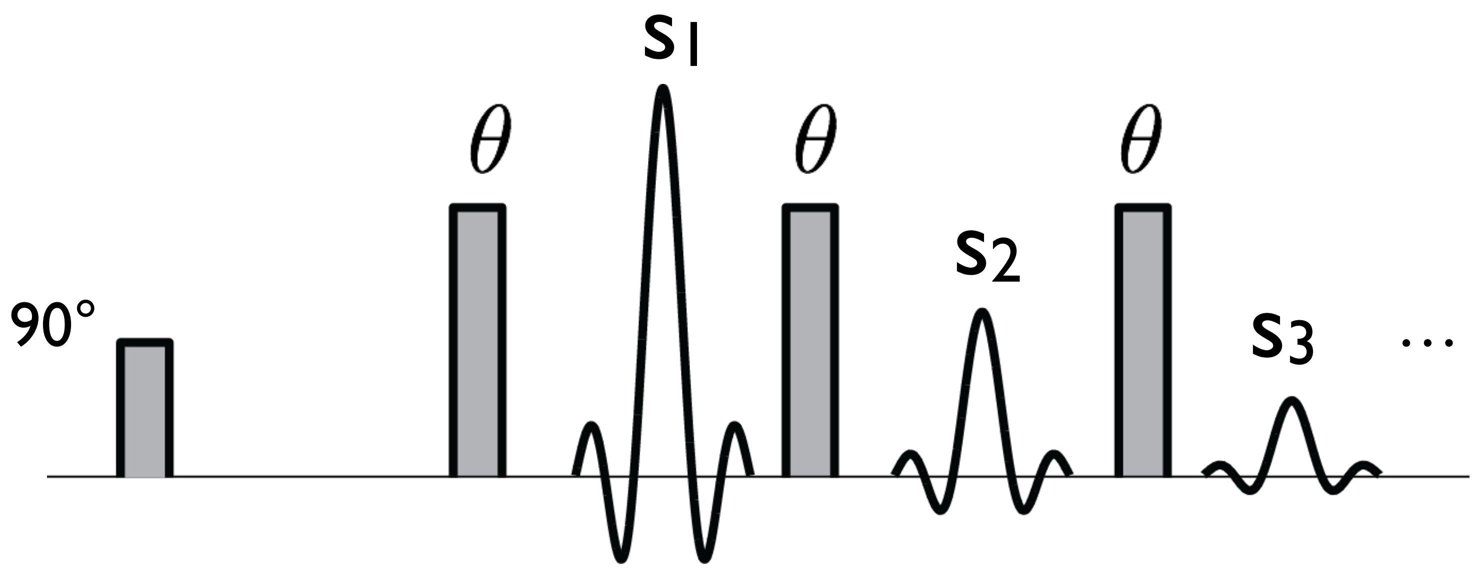

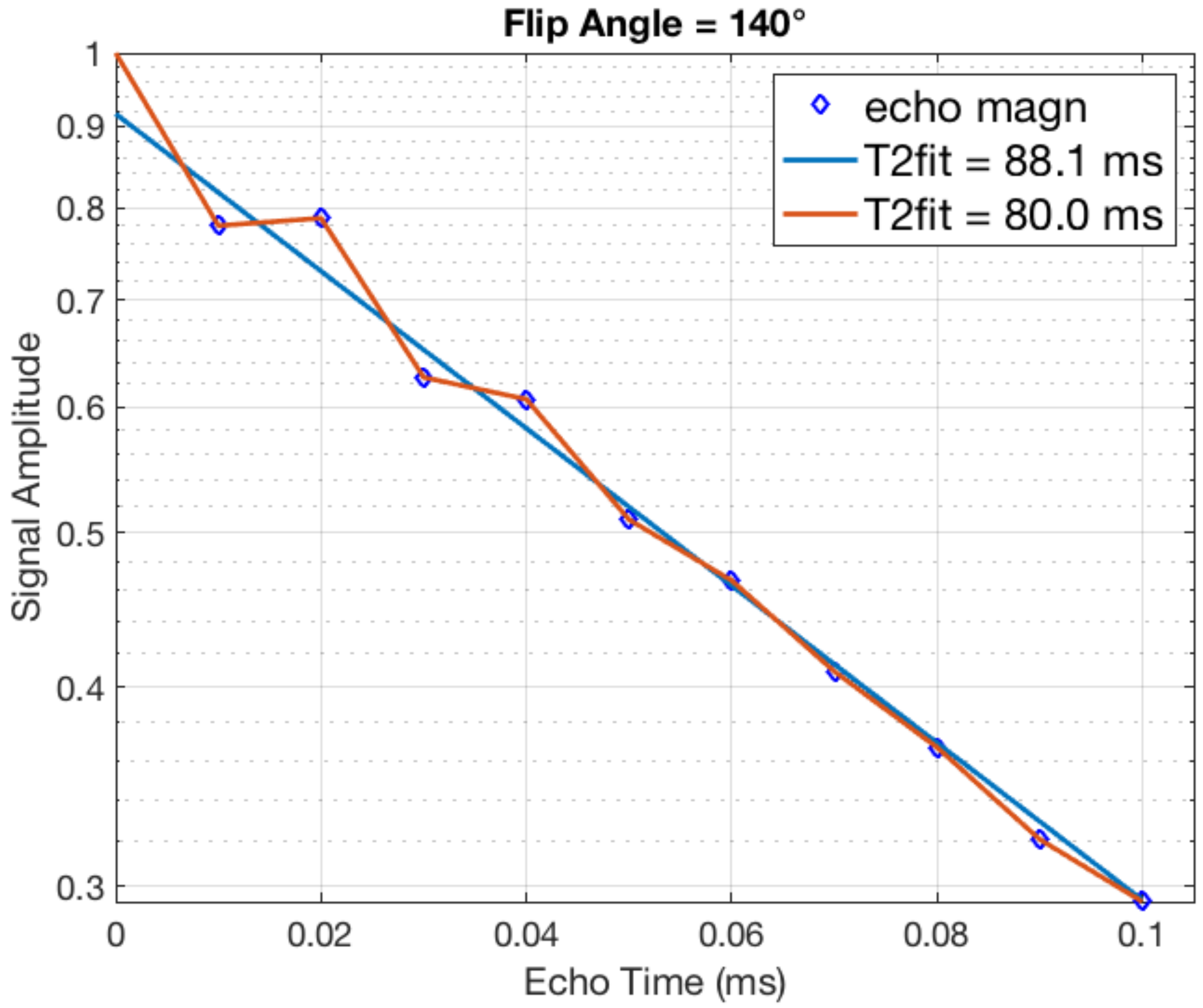

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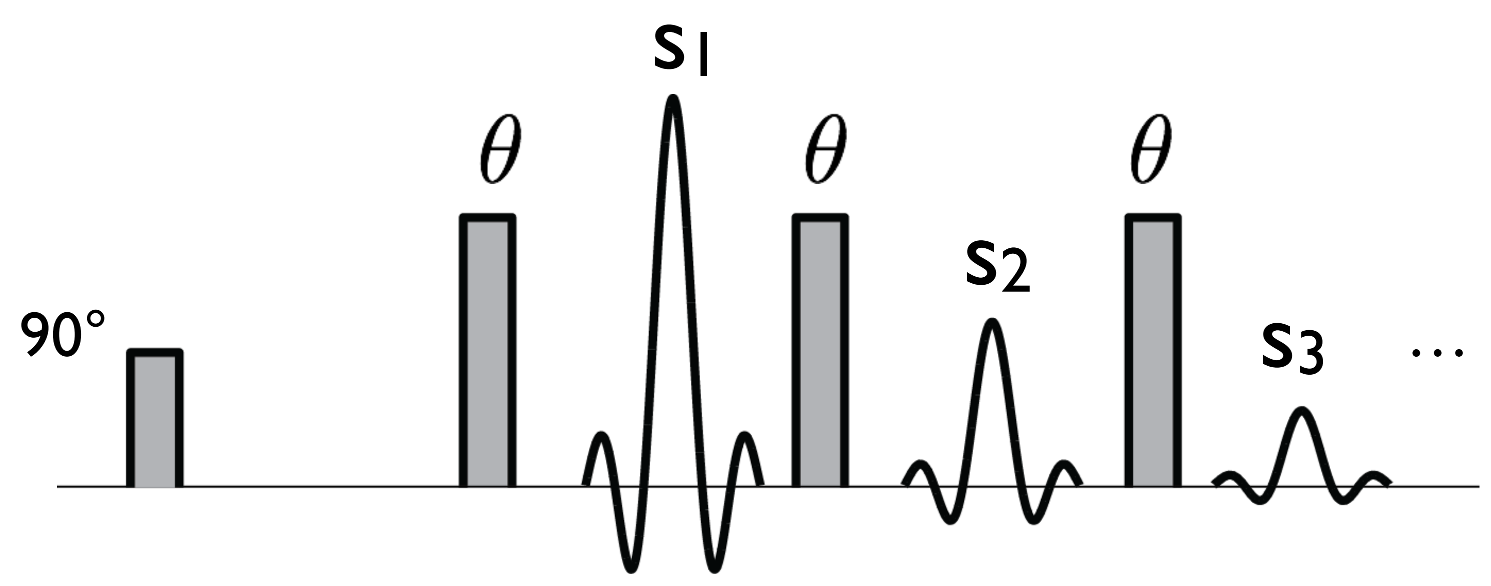
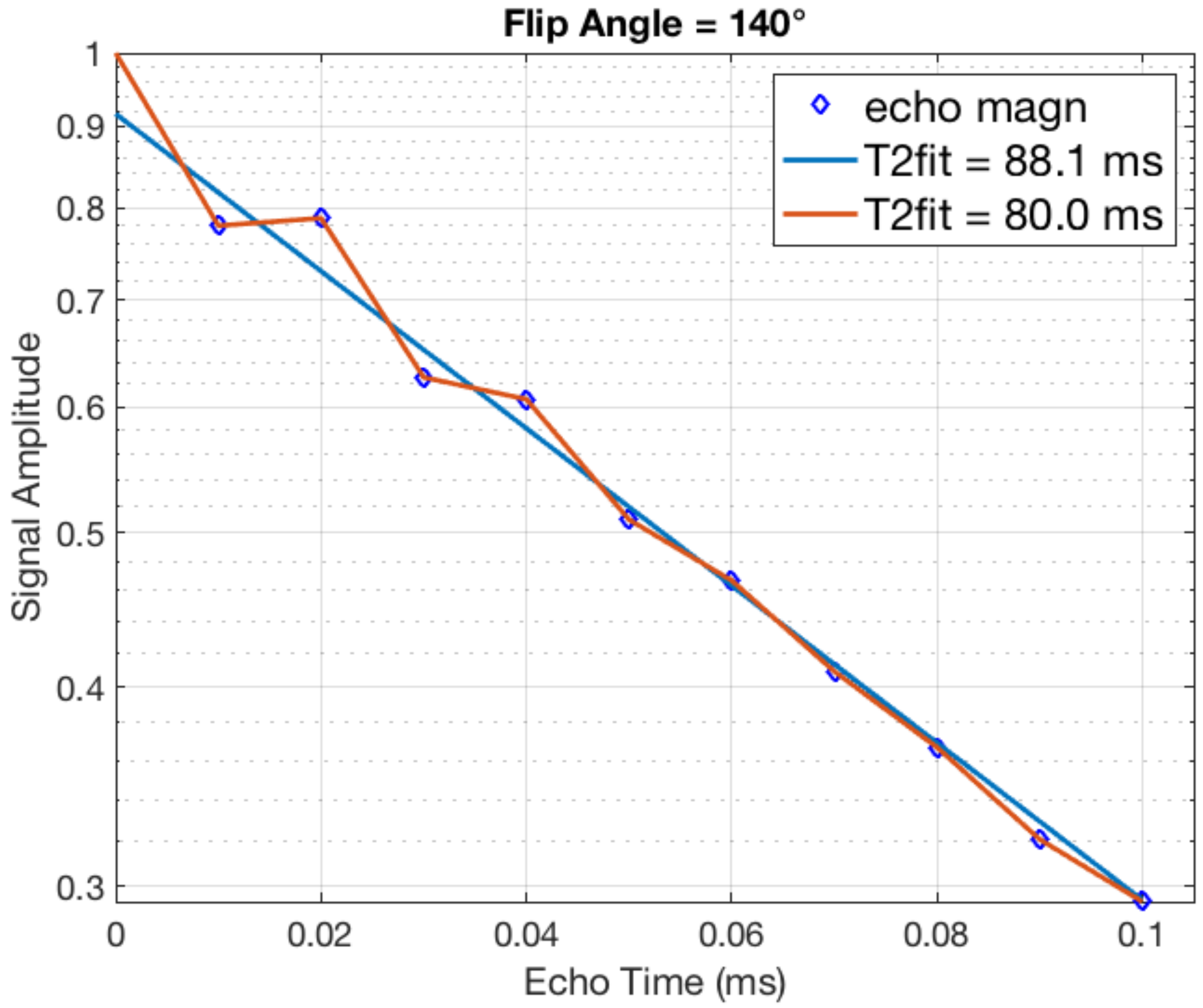
  - Constrain to an assumed or measured value
  - Jointly fit with other parameters





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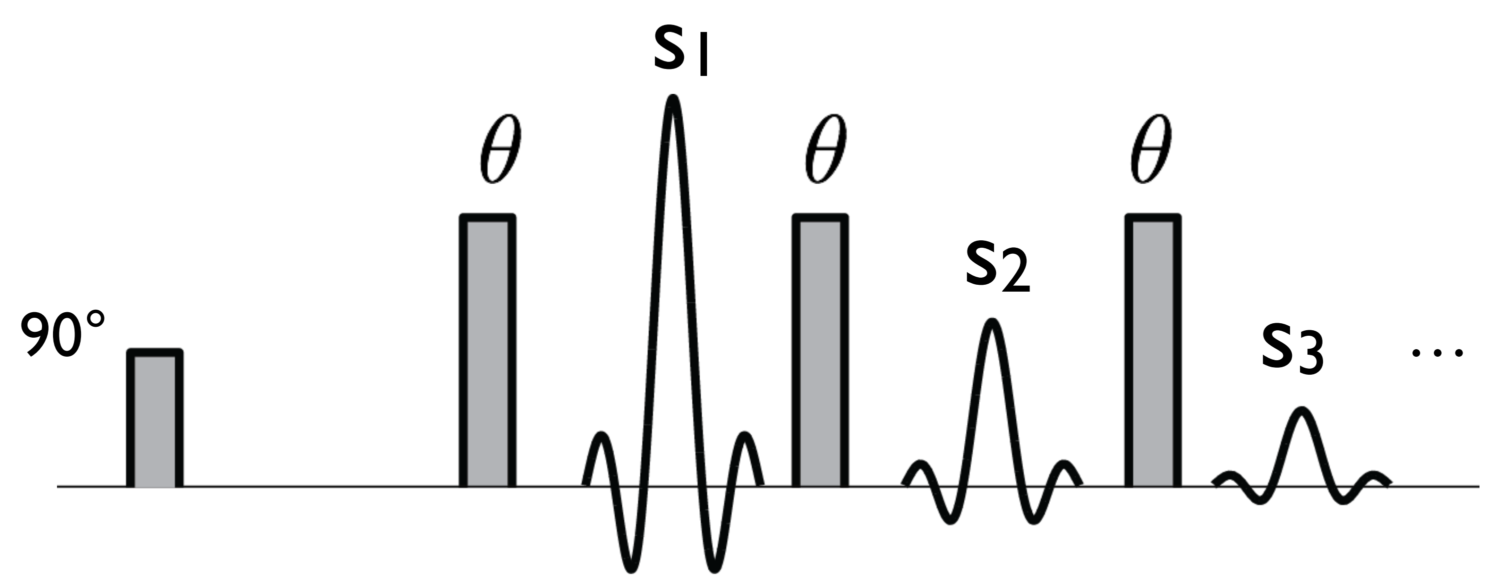
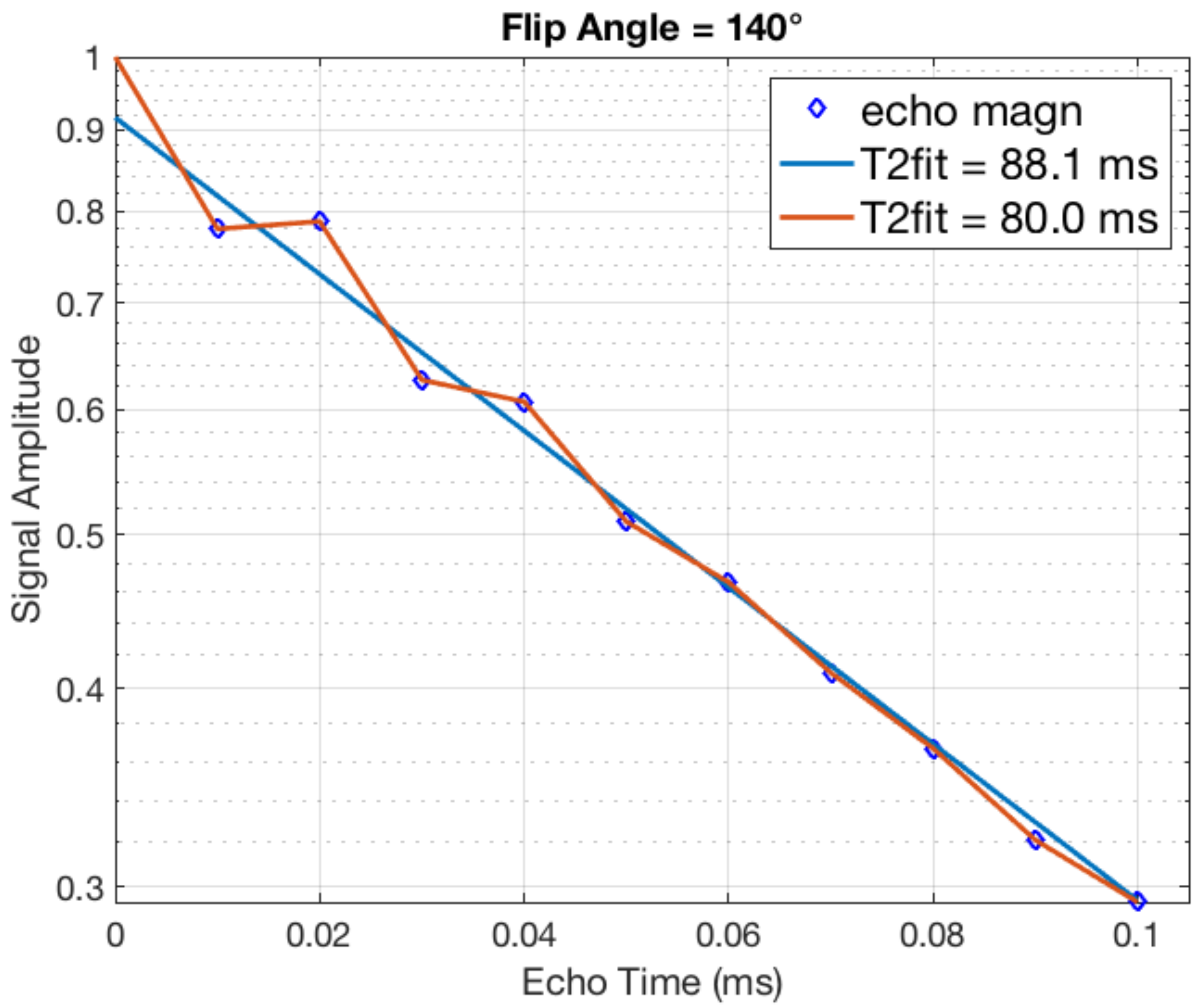
- Objective: measure T_2 via multiple spin echo MRI
- Signal Equation, $s\left(t_e\right) = \mathrm{EPG}\left[t_e; M_0, T_2, \theta\right]$
- Model parameters of interest: M_0, T_2
- Nuisance parameter: θ
  - Constrain to an assumed or measured value
  - Jointly fit with other parameters
- What precision & accuracy in a *measured* $\hat{\theta}$ will result in a lower MSE of $\hat{T}_2$ c/w jointly fitting M_0, T_2, θ?





Propagation of Error

- Three possible sources

Mean Squared Error

$$\boldsymbol{\varepsilon}^{\mathbf{2}}_{\hat{\boldsymbol{\beta}}_{\mathrm{f}}} \approx$$

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  - noise (imprecision) in images

Mean Squared Error

Prop of Image Noise

$$\boldsymbol{\varepsilon}^{\mathbf{2}}_{\hat{\boldsymbol{\beta}}_{\mathrm{f}}} \approx \sigma_{\mathrm{s}}^2 \left(\mathbf{J}_{\boldsymbol{\beta}_{\mathrm{f}}}^{\mathrm{T}} \mathbf{J}_{\boldsymbol{\beta}_{\mathrm{f}}}\right)^{-1} + \ldots$$

Propagation of Error

- Three possible sources
  - noise (imprecision) in images
  - noise (imprecision) in nuisance parameter measurement

Mean Squared Error

Prop of Image Noise

$$\boldsymbol{\varepsilon}^{\mathbf{2}}_{\hat{\boldsymbol{\beta}}_{\mathrm{f}}} \approx \sigma_{\mathrm{s}}^{2}\left(\mathbf{J}_{\boldsymbol{\beta}_{\mathrm{f}}}^{\mathrm{T}}\mathbf{J}_{\boldsymbol{\beta}_{\mathrm{f}}}\right)^{-1} + \ldots$$

Prop of Constraint Noise

$$\frac{\partial\bar{\boldsymbol{\beta}}_{\mathrm{f}}\left(\bar{\boldsymbol{\beta}}_{\mathrm{c}}\right)}{\partial\bar{\boldsymbol{\beta}}_{\mathrm{c}}}\boldsymbol{\Sigma}_{\hat{\boldsymbol{\beta}}_{\mathrm{c}}}\frac{\partial\bar{\boldsymbol{\beta}}_{\mathrm{f}}\left(\bar{\boldsymbol{\beta}}_{\mathrm{c}}\right)^{\mathrm{T}}}{\partial\bar{\boldsymbol{\beta}}_{\mathrm{c}}} + \ldots$$

Propagation of Error

- Three possible sources
  - noise (imprecision) in images
  - noise (imprecision) in nuisance parameter measurement
  - bias (inaccuracy) in nuisance parameter measurement (or assumption)

Mean Squared Error → Prop of Image Noise ↓

$$\boldsymbol{\varepsilon}^{\mathbf{2}}_{\hat{\boldsymbol{\beta}}_{\mathrm{f}}} \approx \sigma_{\mathrm{s}}^{2}\left(\mathbf{J}_{\boldsymbol{\beta}_{\mathrm{f}}}^{\mathrm{T}}\mathbf{J}_{\boldsymbol{\beta}_{\mathrm{f}}}\right)^{-1} + \ldots$$

Prop of Constraint Noise →

$$\frac{\partial\bar{\boldsymbol{\beta}}_{\mathrm{f}}\left(\bar{\boldsymbol{\beta}}_{\mathrm{c}}\right)}{\partial\bar{\boldsymbol{\beta}}_{\mathrm{c}}}\boldsymbol{\Sigma}_{\hat{\boldsymbol{\beta}}_{\mathrm{c}}}\frac{\partial\bar{\boldsymbol{\beta}}_{\mathrm{f}}\left(\bar{\boldsymbol{\beta}}_{\mathrm{c}}\right)^{\mathrm{T}}}{\partial\bar{\boldsymbol{\beta}}_{\mathrm{c}}} + \ldots$$

Prop of Constraint Error →

$$\left(\bar{\boldsymbol{\beta}}_{\mathrm{f}}\left(\bar{\boldsymbol{\beta}}_{\mathrm{c}}\right)-\boldsymbol{\beta}_{\mathrm{f}}\right)\left(\bar{\boldsymbol{\beta}}_{\mathrm{f}}\left(\bar{\boldsymbol{\beta}}_{\mathrm{c}}\right)-\boldsymbol{\beta}_{\mathrm{f}}\right)^{\mathrm{T}}$$

$$\boldsymbol{\varepsilon}^{\mathbf{2}}_{\hat{\boldsymbol{\beta}}_{\mathrm{f}}} \approx \boxed{\sigma_{\mathrm{s}}^2 \left(\mathbf{J}^{\mathrm{T}}_{\boldsymbol{\beta}_{\mathrm{f}}} \mathbf{J}_{\boldsymbol{\beta}_{\mathrm{f}}}\right)^{-1}} + \ldots$$

$$\frac{\partial \bar{\boldsymbol{\beta}}_{\mathrm{f}}\left(\bar{\boldsymbol{\beta}}_{\mathrm{c}}\right)}{\partial \bar{\boldsymbol{\beta}}_{\mathrm{c}}} \boldsymbol{\Sigma}_{\hat{\boldsymbol{\beta}}_{\mathrm{c}}} \frac{\partial \bar{\boldsymbol{\beta}}_{\mathrm{f}}\left(\bar{\boldsymbol{\beta}}_{\mathrm{c}}\right)^{\mathrm{T}}}{\partial \bar{\boldsymbol{\beta}}_{\mathrm{c}}} + \ldots$$

$$\left(\bar{\boldsymbol{\beta}}_{\mathrm{f}}\left(\bar{\boldsymbol{\beta}}_{\mathrm{c}}\right) - \boldsymbol{\beta}_{\mathrm{f}}\right)\left(\bar{\boldsymbol{\beta}}_{\mathrm{f}}\left(\bar{\boldsymbol{\beta}}_{\mathrm{c}}\right) - \boldsymbol{\beta}_{\mathrm{f}}\right)^{\mathrm{T}}$$

Term 1: error from noise in images

- Cramér-Rao bound of variance (in the absence of β_c or if β_c are constrained perfectly)

$$\sigma_{\mathrm{s}}^2 \left(\mathbf{J}^{\mathrm{T}}_{\beta_{\mathrm{f}}} \mathbf{J}_{\beta_{\mathrm{f}}}\right)^{-1}$$

$$\varepsilon^{2}_{\hat{\boldsymbol{\beta}}_{\mathrm{f}}} \approx \sigma_{\mathrm{s}}^{2}\left(\mathbf{J}_{\boldsymbol{\beta}_{\mathrm{f}}}^{\mathrm{T}}\mathbf{J}_{\boldsymbol{\beta}_{\mathrm{f}}}\right)^{-1} + \ldots$$

$$\frac{\partial\bar{\boldsymbol{\beta}}_{\mathrm{f}}\left(\bar{\boldsymbol{\beta}}_{\mathrm{c}}\right)}{\partial\bar{\boldsymbol{\beta}}_{\mathrm{c}}}\boldsymbol{\Sigma}_{\hat{\boldsymbol{\beta}}_{\mathrm{c}}}\frac{\partial\bar{\boldsymbol{\beta}}_{\mathrm{f}}\left(\bar{\boldsymbol{\beta}}_{\mathrm{c}}\right)}{\partial\bar{\boldsymbol{\beta}}_{\mathrm{c}}}^{\mathrm{T}} + \ldots$$

$$\left(\bar{\boldsymbol{\beta}}_{\mathrm{f}}\left(\bar{\boldsymbol{\beta}}_{\mathrm{c}}\right) - \boldsymbol{\beta}_{\mathrm{f}}\right)\left(\bar{\boldsymbol{\beta}}_{\mathrm{f}}\left(\bar{\boldsymbol{\beta}}_{\mathrm{c}}\right) - \boldsymbol{\beta}_{\mathrm{f}}\right)^{\mathrm{T}}$$

Term 1: error from noise in images

- Cramér-Rao bound of variance (in the absence of β_{c} or if β_{c} are constrained perfectly)
- $\mathbf{J}$ is the model jacobian
  - compute partial derivatives for a given set of q and β values
    - analytical or finite-difference

$$\sigma_{\mathrm{s}}^{2}\left(\mathbf{J}_{\beta_{\mathrm{f}}}^{\mathrm{T}}\mathbf{J}_{\beta_{\mathrm{f}}}\right)^{-1}$$

$$\mathbf{J}_{\beta_{\mathrm{f}}} = \begin{bmatrix} \partial s_1/\partial\beta_{\mathrm{f},1} & \ldots & \partial s_1/\partial\beta_{\mathrm{f},\mathrm{M_f}} \\ \vdots & & \vdots \\ \partial s_{\mathrm{N}}/\partial\beta_{\mathrm{f},1} & \ldots & \partial s_{\mathrm{N}}/\partial\beta_{\mathrm{f},\mathrm{M_f}} \end{bmatrix}$$

$$\boldsymbol{\varepsilon}^2_{\hat{\boldsymbol{\beta}}_\mathrm{f}} \approx \sigma_\mathrm{s}^2 \left(\mathbf{J}^\mathrm{T}_{\boldsymbol{\beta}_\mathrm{f}} \mathbf{J}_{\boldsymbol{\beta}_\mathrm{f}}\right)^{-1} + \ldots$$

$$\frac{\partial \bar{\boldsymbol{\beta}}_\mathrm{f}\left(\bar{\boldsymbol{\beta}}_\mathrm{c}\right)}{\partial \bar{\boldsymbol{\beta}}_\mathrm{c}} \boldsymbol{\Sigma}_{\hat{\boldsymbol{\beta}}_\mathrm{c}} \frac{\partial \bar{\boldsymbol{\beta}}_\mathrm{f}\left(\bar{\boldsymbol{\beta}}_\mathrm{c}\right)}{\partial \bar{\boldsymbol{\beta}}_\mathrm{c}}^\mathrm{T} + \ldots$$

$$\left(\bar{\boldsymbol{\beta}}_\mathrm{f}\left(\bar{\boldsymbol{\beta}}_\mathrm{c}\right) - \boldsymbol{\beta}_\mathrm{f}\right)\left(\bar{\boldsymbol{\beta}}_\mathrm{f}\left(\bar{\boldsymbol{\beta}}_\mathrm{c}\right) - \boldsymbol{\beta}_\mathrm{f}\right)^\mathrm{T}$$

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    - analytical or finite-difference
- for T_2 example

$$\sigma_\mathrm{S}^2 \left(\mathbf{J}^\mathrm{T}_{\beta_\mathrm{f}} \mathbf{J}_{\beta_\mathrm{f}}\right)^{-1}$$

$$\mathbf{J}_{\beta_\mathrm{f}} = \begin{bmatrix} \partial s_1 / \partial \beta_{\mathrm{f},1} & \ldots & \partial s_1 / \partial \beta_{\mathrm{f},\mathrm{M_f}} \\ \vdots & & \vdots \\ \partial s_\mathrm{N} / \partial \beta_{\mathrm{f},1} & \ldots & \partial s_\mathrm{N} / \partial \beta_{\mathrm{f},\mathrm{M_f}} \end{bmatrix}$$

$$\partial \mathrm{EPG}\left[t_\mathrm{e}; M_0, T_2, \theta\right] / \partial M_0$$

$$\partial \mathrm{EPG}\left[t_\mathrm{e}; M_0, T_2, \theta\right] / \partial T_2$$

Term II: error from noise in nuisance parameter maps

$$\boldsymbol{\varepsilon}^{\mathbf{2}}_{\hat{\boldsymbol{\beta}}_\mathrm{f}} \approx \sigma_\mathrm{s}^2 \left(\mathbf{J}_{\boldsymbol{\beta}_\mathrm{f}}^\mathrm{T} \mathbf{J}_{\boldsymbol{\beta}_\mathrm{f}}\right)^{-1} + \ldots$$
$$\frac{\partial \bar{\boldsymbol{\beta}}_\mathrm{f}\left(\bar{\boldsymbol{\beta}}_\mathrm{c}\right)}{\partial \bar{\boldsymbol{\beta}}_\mathrm{c}} \boldsymbol{\Sigma}_{\hat{\boldsymbol{\beta}}_\mathrm{c}} \frac{\partial \bar{\boldsymbol{\beta}}_\mathrm{f}\left(\bar{\boldsymbol{\beta}}_\mathrm{c}\right)}{\partial \bar{\boldsymbol{\beta}}_\mathrm{c}}^\mathrm{T} + \ldots$$
$$\left(\bar{\boldsymbol{\beta}}_\mathrm{f}\left(\bar{\boldsymbol{\beta}}_\mathrm{c}\right) - \boldsymbol{\beta}_\mathrm{f}\right)\left(\bar{\boldsymbol{\beta}}_\mathrm{f}\left(\bar{\boldsymbol{\beta}}_\mathrm{c}\right) - \boldsymbol{\beta}_\mathrm{f}\right)^\mathrm{T}$$

- first-order propagation-of-error from $\hat{\beta}_\mathrm{c}$ to $\hat{\beta}_\mathrm{f}$

Term II: error from noise in nuisance parameter maps

$$\boldsymbol{\varepsilon}^{\mathbf{2}}_{\hat{\boldsymbol{\beta}}_{\mathrm{f}}} \approx \sigma_{\mathrm{s}}^2 \left(\mathbf{J}^{\mathrm{T}}_{\boldsymbol{\beta}_{\mathrm{f}}} \mathbf{J}_{\boldsymbol{\beta}_{\mathrm{f}}}\right)^{-1} + \ldots$$

$$\boxed{\frac{\partial \bar{\boldsymbol{\beta}}_{\mathrm{f}}\left(\bar{\boldsymbol{\beta}}_{\mathrm{c}}\right)}{\partial \bar{\boldsymbol{\beta}}_{\mathrm{c}}} \boldsymbol{\Sigma}_{\hat{\boldsymbol{\beta}}_{\mathrm{c}}} \frac{\partial \bar{\boldsymbol{\beta}}_{\mathrm{f}}\left(\bar{\boldsymbol{\beta}}_{\mathrm{c}}\right)}{\partial \bar{\boldsymbol{\beta}}_{\mathrm{c}}}^{\mathrm{T}}} + \ldots$$

$$\left(\bar{\boldsymbol{\beta}}_{\mathrm{f}}\left(\bar{\boldsymbol{\beta}}_{\mathrm{c}}\right) - \boldsymbol{\beta}_{\mathrm{f}}\right)\left(\bar{\boldsymbol{\beta}}_{\mathrm{f}}\left(\bar{\boldsymbol{\beta}}_{\mathrm{c}}\right) - \boldsymbol{\beta}_{\mathrm{f}}\right)^{\mathrm{T}}$$

- first-order propagation-of-error from $\hat{\beta}_{\mathrm{c}}$ to $\hat{\beta}_{\mathrm{f}}$
- the noise covariance of nuisance parameters
  - zero if β_{c} are assumed

$$\Sigma_{\hat{\beta}_{\mathrm{c}}} = \begin{bmatrix} \sigma^2_{\hat{\beta}_{\mathrm{c1}}} & \cdots & \sigma^2_{\hat{\beta}_{\mathrm{c1}}\hat{\beta}_{\mathrm{cM_c}}} \\ \vdots & & \vdots \\ \sigma^2_{\hat{\beta}_{\mathrm{c1}}\hat{\beta}_{\mathrm{cM_c}}} & \cdots & \sigma^2_{\hat{\beta}_{\mathrm{cM_c}}} \end{bmatrix}$$

Term II: error from noise in nuisance parameter maps

$$\boldsymbol{\varepsilon}^{\mathbf{2}}_{\hat{\boldsymbol{\beta}}_\mathrm{f}} \approx \sigma_\mathrm{s}^2 \left(\mathbf{J}^\mathrm{T}_{\boldsymbol{\beta}_\mathrm{f}} \mathbf{J}_{\boldsymbol{\beta}_\mathrm{f}}\right)^{-1} + \ldots$$

$$\frac{\partial \bar{\boldsymbol{\beta}}_\mathrm{f}\left(\bar{\boldsymbol{\beta}}_\mathrm{c}\right)}{\partial \bar{\boldsymbol{\beta}}_\mathrm{c}} \boldsymbol{\Sigma}_{\hat{\boldsymbol{\beta}}_\mathrm{c}} \frac{\partial \bar{\boldsymbol{\beta}}_\mathrm{f}\left(\bar{\boldsymbol{\beta}}_\mathrm{c}\right)}{\partial \bar{\boldsymbol{\beta}}_\mathrm{c}}^\mathrm{T} + \ldots$$

$$\left(\bar{\boldsymbol{\beta}}_\mathrm{f}\left(\bar{\boldsymbol{\beta}}_\mathrm{c}\right) - \boldsymbol{\beta}_\mathrm{f}\right)\left(\bar{\boldsymbol{\beta}}_\mathrm{f}\left(\bar{\boldsymbol{\beta}}_\mathrm{c}\right) - \boldsymbol{\beta}_\mathrm{f}\right)^\mathrm{T}$$

- first-order propagation-of-error from $\hat{\beta}_\mathrm{c}$ to $\hat{\beta}_\mathrm{f}$
- the noise covariance of nuisance parameters
  - zero if β_c are assumed
- the average fitted parameters for given average nuisance parameters

$$\Sigma_{\hat{\beta}_\mathrm{c}} = \begin{bmatrix} \sigma^2_{\hat{\beta}_{\mathrm{c}1}} & \cdots & \sigma^2_{\hat{\beta}_{\mathrm{c}1}\hat{\beta}_{\mathrm{cM_c}}} \\ \vdots & & \vdots \\ \sigma^2_{\hat{\beta}_{\mathrm{c}1}\hat{\beta}_{\mathrm{cM_c}}} & \cdots & \sigma^2_{\hat{\beta}_{\mathrm{cM_c}}} \end{bmatrix}$$

$$\bar{\beta}_\mathrm{f}\left(\bar{\beta}_\mathrm{c}\right)$$

Term 11: error from noise in nuisance parameter maps

$$\boldsymbol{\varepsilon}^{\mathbf{2}}_{\hat{\boldsymbol{\beta}}_\mathrm{f}} \approx \sigma_\mathrm{s}^2 \left(\mathbf{J}^\mathrm{T}_{\boldsymbol{\beta}_\mathrm{f}} \mathbf{J}_{\boldsymbol{\beta}_\mathrm{f}}\right)^{-1} + \ldots$$

$$\boxed{\frac{\partial \bar{\boldsymbol{\beta}}_\mathrm{f}\left(\bar{\boldsymbol{\beta}}_\mathrm{c}\right)}{\partial \bar{\boldsymbol{\beta}}_\mathrm{c}} \boldsymbol{\Sigma}_{\hat{\boldsymbol{\beta}}_\mathrm{c}} \frac{\partial \bar{\boldsymbol{\beta}}_\mathrm{f}\left(\bar{\boldsymbol{\beta}}_\mathrm{c}\right)}{\partial \bar{\boldsymbol{\beta}}_\mathrm{c}}^\mathrm{T}} + \ldots$$

$$\left(\bar{\boldsymbol{\beta}}_\mathrm{f}\left(\bar{\boldsymbol{\beta}}_\mathrm{c}\right) - \boldsymbol{\beta}_\mathrm{f}\right)\left(\bar{\boldsymbol{\beta}}_\mathrm{f}\left(\bar{\boldsymbol{\beta}}_\mathrm{c}\right) - \boldsymbol{\beta}_\mathrm{f}\right)^\mathrm{T}$$

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$$\frac{\partial \bar{\beta}_\mathrm{f}\left(\bar{\beta}_\mathrm{c}\right)}{\partial \bar{\beta}_\mathrm{c}} = \begin{bmatrix} \partial\bar{\beta}_\mathrm{f1}/\partial\bar{\beta}_\mathrm{c1} & \cdots & \partial\bar{\beta}_\mathrm{f1}/\partial\bar{\beta}_{\mathrm{cM_c}} \\ \vdots & & \vdots \\ \partial\bar{\beta}_{\mathrm{fM_f}}/\partial\bar{\beta}_\mathrm{c1} & \cdots & \partial\bar{\beta}_{\mathrm{fM_f}}/\partial\bar{\beta}_{\mathrm{cM_c}} \end{bmatrix}$$

Term II: error from noise in nuisance parameter maps

$$\boldsymbol{\varepsilon}^{\mathbf{2}}_{\hat{\boldsymbol{\beta}}_{\mathrm{f}}} \approx \sigma_{\mathrm{s}}^2 \left(\mathbf{J}^{\mathrm{T}}_{\boldsymbol{\beta}_{\mathrm{f}}} \mathbf{J}_{\boldsymbol{\beta}_{\mathrm{f}}}\right)^{-1} + \ldots$$

$$\boxed{\frac{\partial \bar{\boldsymbol{\beta}}_{\mathrm{f}}\left(\bar{\boldsymbol{\beta}}_{\mathrm{c}}\right)}{\partial \bar{\boldsymbol{\beta}}_{\mathrm{c}}} \boldsymbol{\Sigma}_{\hat{\boldsymbol{\beta}}_{\mathrm{c}}} \frac{\partial \bar{\boldsymbol{\beta}}_{\mathrm{f}}\left(\bar{\boldsymbol{\beta}}_{\mathrm{c}}\right)}{\partial \bar{\boldsymbol{\beta}}_{\mathrm{c}}}^{\mathrm{T}}} + \ldots$$

$$\left(\bar{\boldsymbol{\beta}}_{\mathrm{f}}\left(\bar{\boldsymbol{\beta}}_{\mathrm{c}}\right) - \boldsymbol{\beta}_{\mathrm{f}}\right)\left(\bar{\boldsymbol{\beta}}_{\mathrm{f}}\left(\bar{\boldsymbol{\beta}}_{\mathrm{c}}\right) - \boldsymbol{\beta}_{\mathrm{f}}\right)^{\mathrm{T}}$$

For the T_2 example

- compute $\sigma^2_{\hat{\theta}}$ by CRB evaluation of B_1 mapping method

$$\Sigma_{\hat{\beta}_{\mathrm{c}}} = \sigma^2_{\hat{\theta}}$$

Term II: error from noise in nuisance parameter maps

$$\boldsymbol{\varepsilon}^{\mathbf{2}}_{\hat{\boldsymbol{\beta}}_{\mathrm{f}}} \approx \sigma_{\mathrm{s}}^2 \left(\mathbf{J}_{\boldsymbol{\beta}_{\mathrm{f}}}^{\mathrm{T}} \mathbf{J}_{\boldsymbol{\beta}_{\mathrm{f}}}\right)^{-1} + \ldots$$

$$\boxed{\frac{\partial \bar{\boldsymbol{\beta}}_{\mathrm{f}}\left(\bar{\boldsymbol{\beta}}_{\mathrm{c}}\right)}{\partial \bar{\boldsymbol{\beta}}_{\mathrm{c}}} \boldsymbol{\Sigma}_{\hat{\boldsymbol{\beta}}_{\mathrm{c}}} \frac{\partial \bar{\boldsymbol{\beta}}_{\mathrm{f}}\left(\bar{\boldsymbol{\beta}}_{\mathrm{c}}\right)}{\partial \bar{\boldsymbol{\beta}}_{\mathrm{c}}}^{\mathrm{T}}} + \ldots$$

$$\left(\bar{\boldsymbol{\beta}}_{\mathrm{f}}\left(\bar{\boldsymbol{\beta}}_{\mathrm{c}}\right) - \boldsymbol{\beta}_{\mathrm{f}}\right)\left(\bar{\boldsymbol{\beta}}_{\mathrm{f}}\left(\bar{\boldsymbol{\beta}}_{\mathrm{c}}\right) - \boldsymbol{\beta}_{\mathrm{f}}\right)^{\mathrm{T}}$$

For the T_2 example

- compute $\sigma^2_{\hat{\theta}}$ by CRB evaluation of B_1 mapping method
- compute $T_2(\theta)$ and $M_0(\theta)$ from noiseless images
  - partial derivate estimated by finite difference approximation across θ

$$\Sigma_{\hat{\beta}_{\mathrm{c}}} = \sigma^2_{\hat{\theta}}$$

$$\frac{\partial \bar{\beta}_{\mathrm{f}}\left(\bar{\beta}_{\mathrm{c}}\right)}{\partial \bar{\beta}_{\mathrm{c}}} = \begin{bmatrix} \partial \bar{T}_2 / \partial \bar{\theta} \\ \partial \bar{M}_0 / \partial \bar{\theta} \end{bmatrix}$$

Term II: error from noise in nuisance parameter maps

$$\boldsymbol{\varepsilon}^{\mathbf{2}}_{\hat{\boldsymbol{\beta}}_{\mathrm{f}}} \approx \sigma_{\mathrm{s}}^2 \left(\mathbf{J}^{\mathrm{T}}_{\boldsymbol{\beta}_{\mathrm{f}}} \mathbf{J}_{\boldsymbol{\beta}_{\mathrm{f}}}\right)^{-1} + \dots$$

$$\boxed{\frac{\partial \bar{\boldsymbol{\beta}}_{\mathrm{f}}\left(\bar{\boldsymbol{\beta}}_{\mathrm{c}}\right)}{\partial \bar{\boldsymbol{\beta}}_{\mathrm{c}}} \boldsymbol{\Sigma}_{\hat{\boldsymbol{\beta}}_{\mathrm{c}}} \frac{\partial \bar{\boldsymbol{\beta}}_{\mathrm{f}}\left(\bar{\boldsymbol{\beta}}_{\mathrm{c}}\right)}{\partial \bar{\boldsymbol{\beta}}_{\mathrm{c}}}^{\mathrm{T}}} + \dots$$

$$\left(\bar{\boldsymbol{\beta}}_{\mathrm{f}}\left(\bar{\boldsymbol{\beta}}_{\mathrm{c}}\right) - \boldsymbol{\beta}_{\mathrm{f}}\right)\left(\bar{\boldsymbol{\beta}}_{\mathrm{f}}\left(\bar{\boldsymbol{\beta}}_{\mathrm{c}}\right) - \boldsymbol{\beta}_{\mathrm{f}}\right)^{\mathrm{T}}$$

For the T_2 example

- compute $\sigma^2_{\hat{\theta}}$ by CRB evaluation of B_1 mapping method

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- compute $T_2(\theta)$ and $M_0(\theta)$ from noiseless images
  - partial derivate estimated by finite difference approximation across θ

$$\frac{\partial \bar{\beta}_{\mathrm{f}}\left(\bar{\beta}_{\mathrm{c}}\right)}{\partial \bar{\beta}_{\mathrm{c}}} = \begin{bmatrix} \partial \bar{T}_2 / \partial \bar{\theta} \\ \partial \bar{M}_0 / \partial \bar{\theta} \end{bmatrix}$$

- if we only care about errors in fitted T_2, term II reduces to →

$$\sigma^2_{\hat{\theta}} \left(\partial \bar{T}_2 / \partial \bar{\theta}\right)^2$$

Term III: error from bias in nuisance parameter maps

$$\boldsymbol{\varepsilon}^{\mathbf{2}}_{\hat{\boldsymbol{\beta}}_\mathrm{f}} \approx \sigma_\mathrm{s}^2 \left(\mathbf{J}^\mathrm{T}_{\boldsymbol{\beta}_\mathrm{f}} \mathbf{J}_{\boldsymbol{\beta}_\mathrm{f}}\right)^{-1} + \ldots$$

$$\frac{\partial \bar{\boldsymbol{\beta}}_\mathrm{f}\left(\bar{\boldsymbol{\beta}}_\mathrm{c}\right)}{\partial \bar{\boldsymbol{\beta}}_\mathrm{c}} \boldsymbol{\Sigma}_{\hat{\boldsymbol{\beta}}_\mathrm{c}} \frac{\partial \bar{\boldsymbol{\beta}}_\mathrm{f}\left(\bar{\boldsymbol{\beta}}_\mathrm{c}\right)}{\partial \bar{\boldsymbol{\beta}}_\mathrm{c}}^\mathrm{T} + \ldots$$

$$\left(\bar{\boldsymbol{\beta}}_\mathrm{f}\left(\bar{\boldsymbol{\beta}}_\mathrm{c}\right) - \boldsymbol{\beta}_\mathrm{f}\right)\left(\bar{\boldsymbol{\beta}}_\mathrm{f}\left(\bar{\boldsymbol{\beta}}_\mathrm{c}\right) - \boldsymbol{\beta}_\mathrm{f}\right)^\mathrm{T}$$

- bias in fitted parameters

$$\bar{\beta}_\mathrm{f}\left(\bar{\beta}_\mathrm{c}\right) - \beta_\mathrm{f}$$

Term III: error from bias in nuisance parameter maps

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$$\left(\bar{\boldsymbol{\beta}}_\mathrm{f}\left(\bar{\boldsymbol{\beta}}_\mathrm{c}\right) - \boldsymbol{\beta}_\mathrm{f}\right)\left(\bar{\boldsymbol{\beta}}_\mathrm{f}\left(\bar{\boldsymbol{\beta}}_\mathrm{c}\right) - \boldsymbol{\beta}_\mathrm{f}\right)^\mathrm{T}$$

- bias in fitted parameters

$$\bar{\beta}_\mathrm{f}\left(\bar{\beta}_\mathrm{c}\right) - \beta_\mathrm{f}$$

- squared error

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- again, considering only error in fitted T_2, term III is →

$$\left(\bar{T}_2\left(\bar{\theta}\right) - T_2\right)^2$$

T_2 Example Calculations

- Image SNR = 100, T_2 = 20-200 ms, NE/ESP = 32/10 ms and 4/30 ms

Example Results: Precision

- image SNR = 100, T_2 = 80 ms, NE/ESP = 32/10 ms and 4/30 ms
- accurate measures of θ (terms I and II only) or jointly fitted M_0, T_2, and θ

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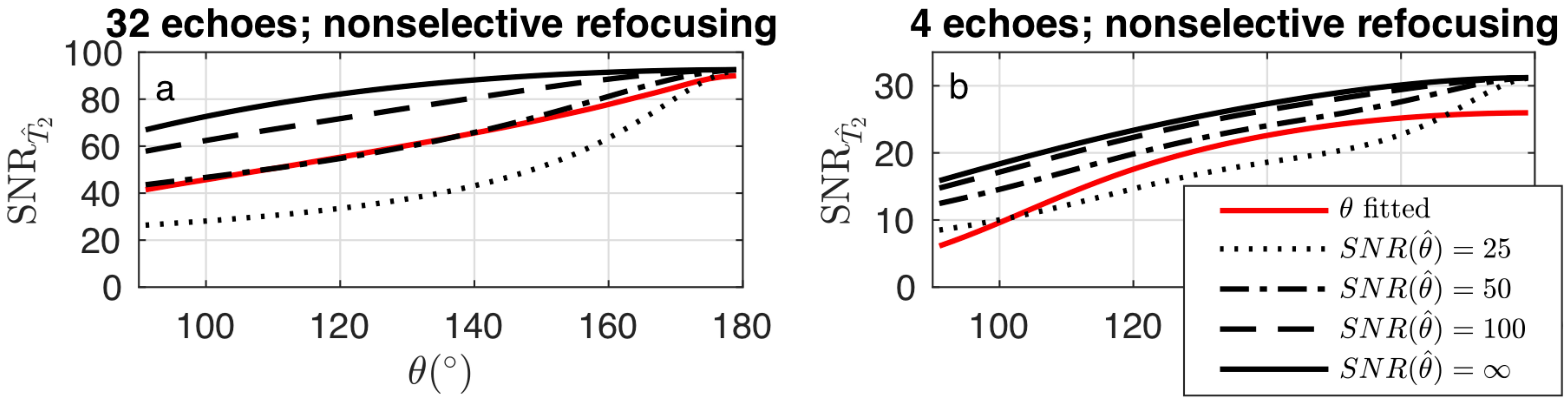
- image SNR = 100, T_2 = 80 ms, NE/ESP = 32/10 ms and 4/30 ms
- accurate measures of θ (terms I and II only) or jointly fitted M_0, T_2, and θ
- if SNR(θ) > 1/2 image SNR, use measure θ



Example Results: Accuracy

- image SNR = 100, T_2 = 80 ms, NE/ESP = 32/10 ms and 4/30 ms
- noiseless calculations, bias in $\hat{\theta}$ (term III only)

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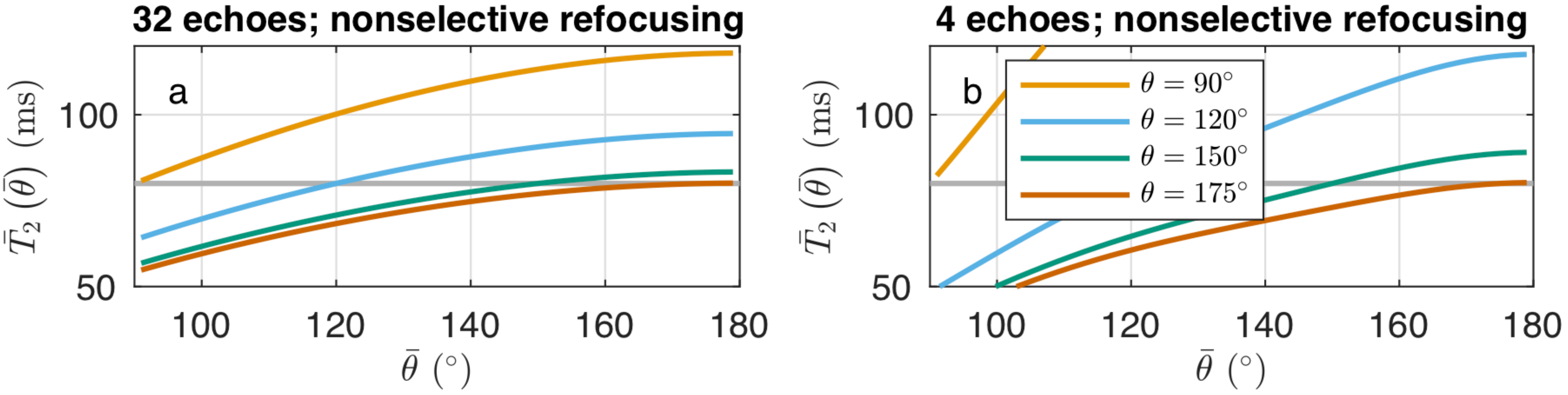
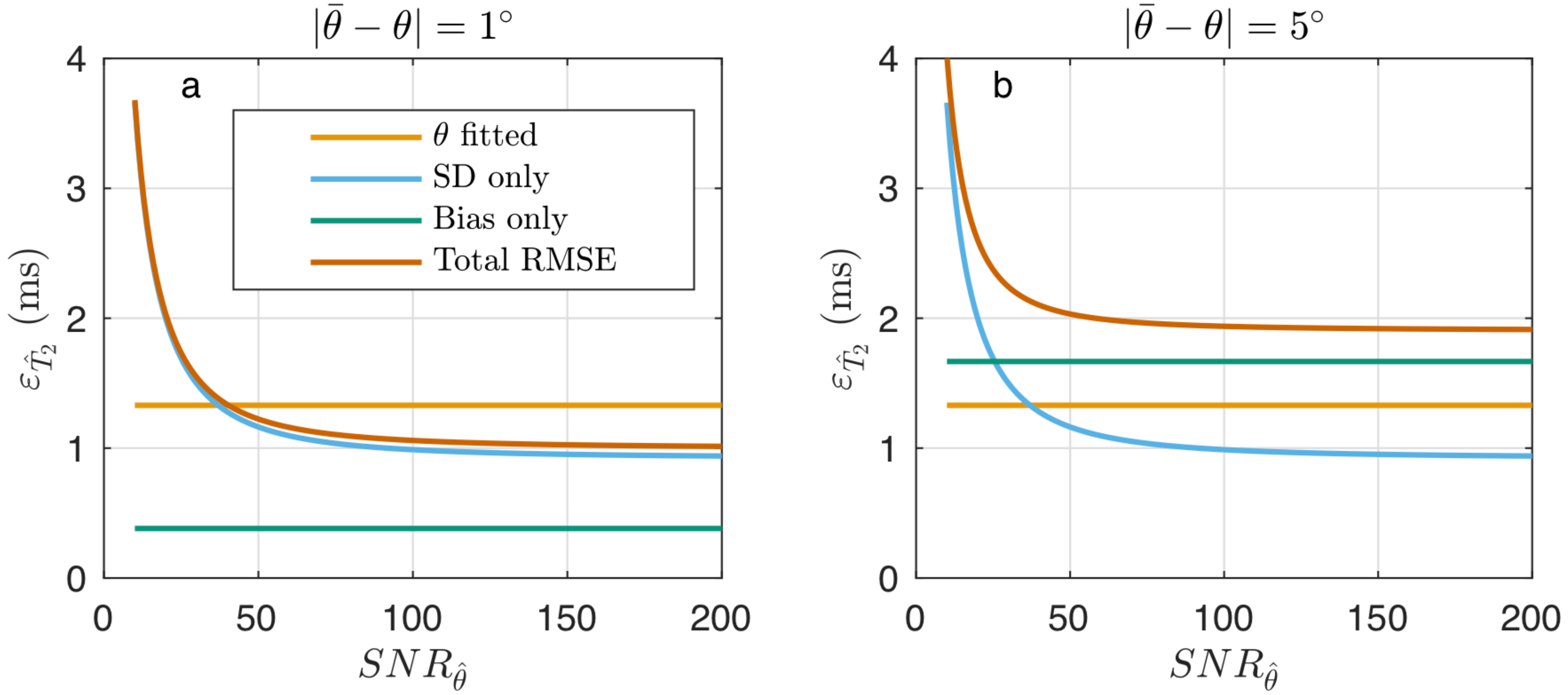
- image SNR = 100, T_2 = 80 ms, NE/ESP = 32/10 ms and 4/30 ms
- noiseless calculations, bias in $\hat{\theta}$ (term III only)
- bias in fitted T_2 is smallest for large θ (and small θ bias); worse for fewer echoes

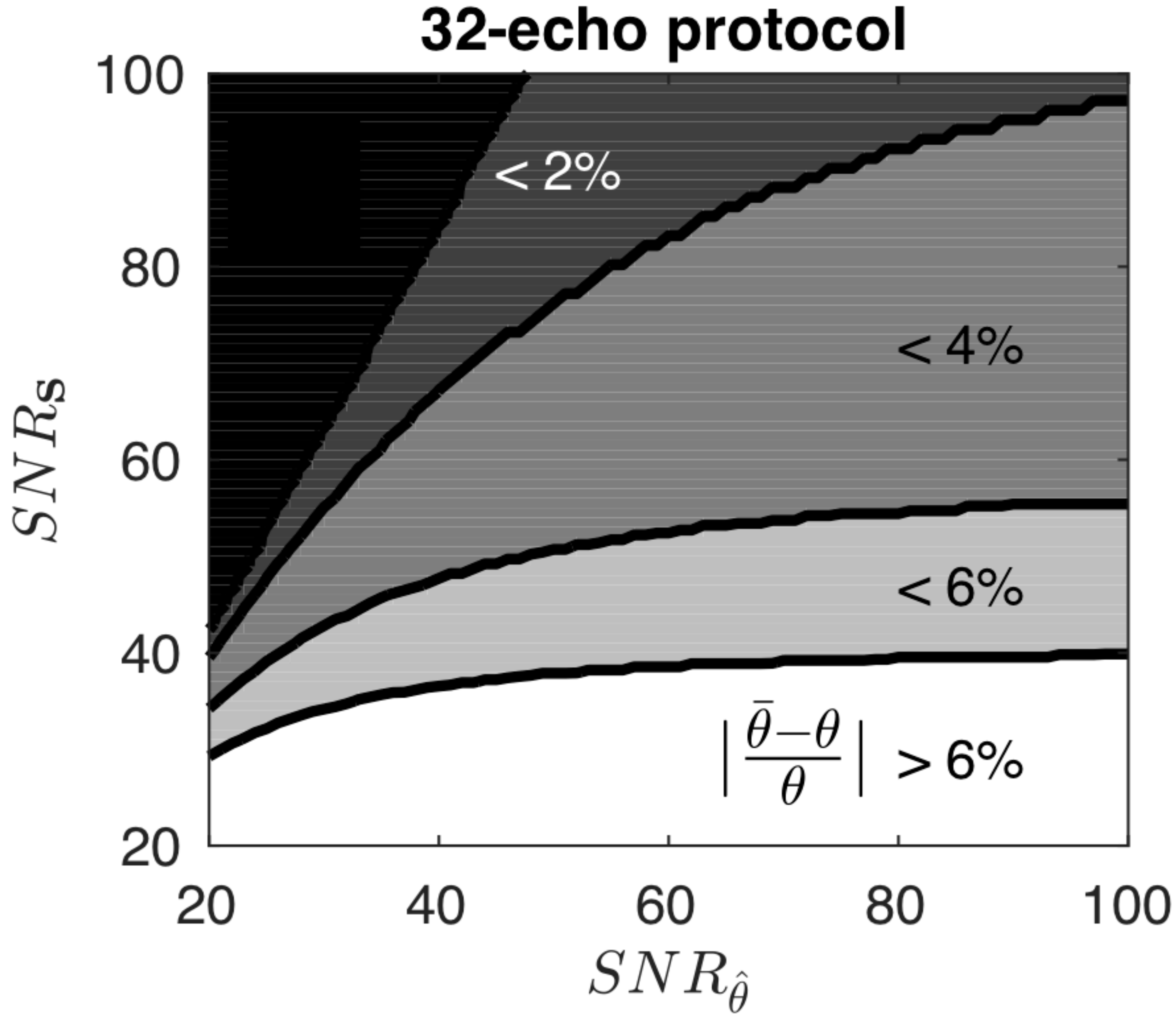


Example Results: Mean Squared Error



Example Results: Bias Threshold

- maximum $\hat{\theta}$-bias that allows reduced MSE(T_2) by measuring θ
- example results for θ = 150° and T_2 = 80 ms
- If image SNR is high
  - need low $\hat{\theta}$-bias,
  - need unbiased $\hat{\theta}$ if SNR($\hat{\theta}$) $\leq$ 1/2 SNR(image)
- E.g., SNR(image) = 60



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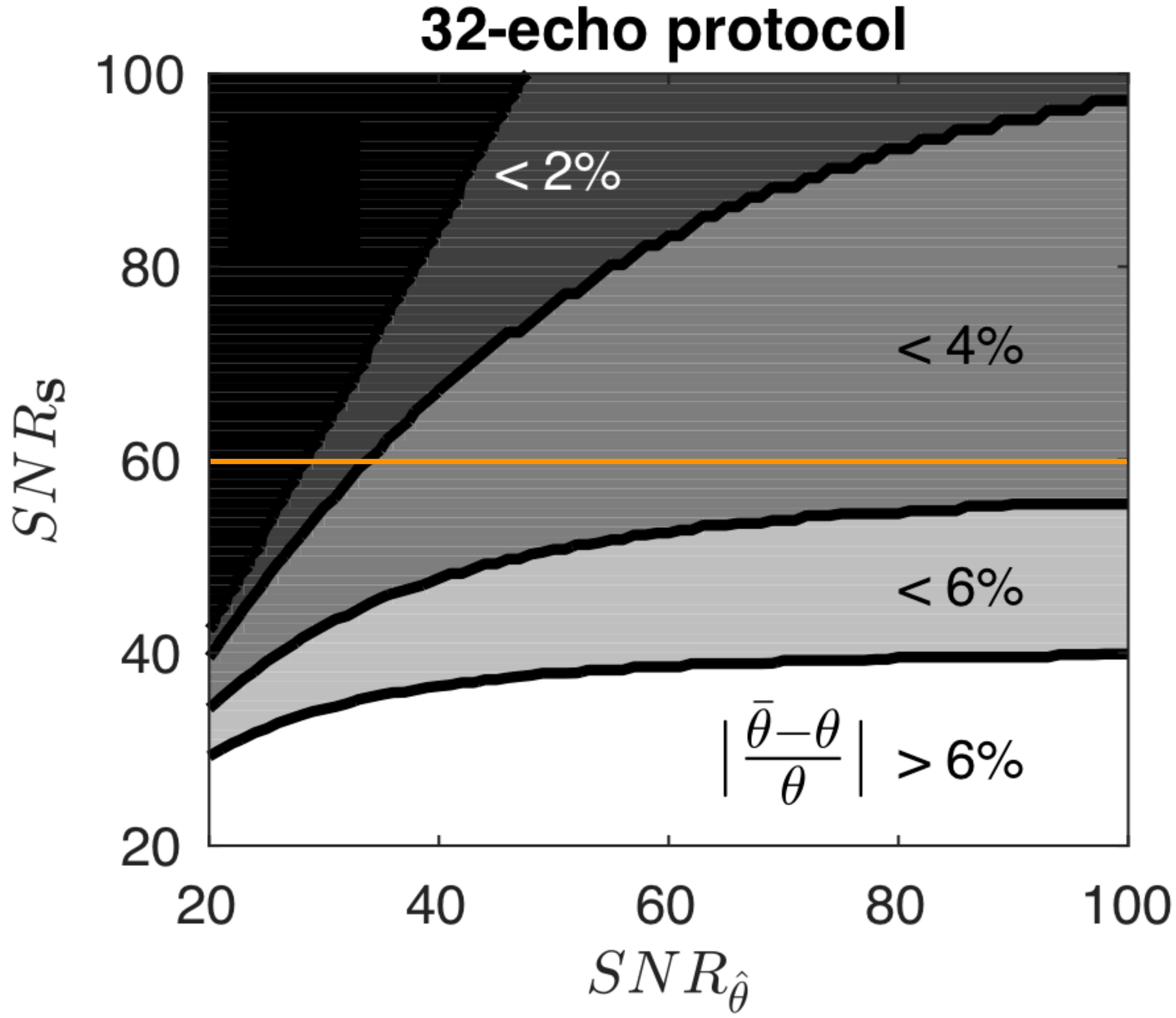

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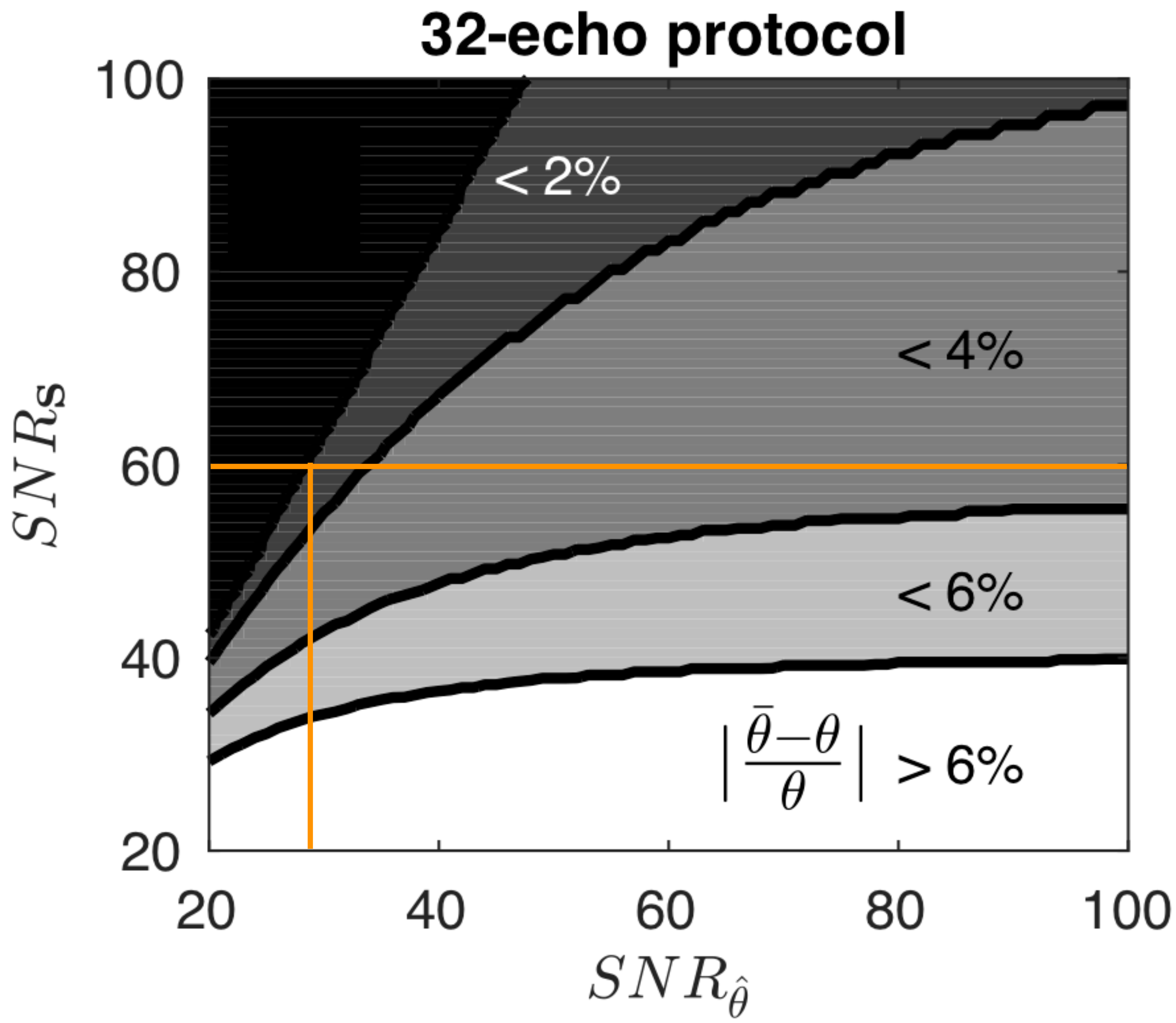

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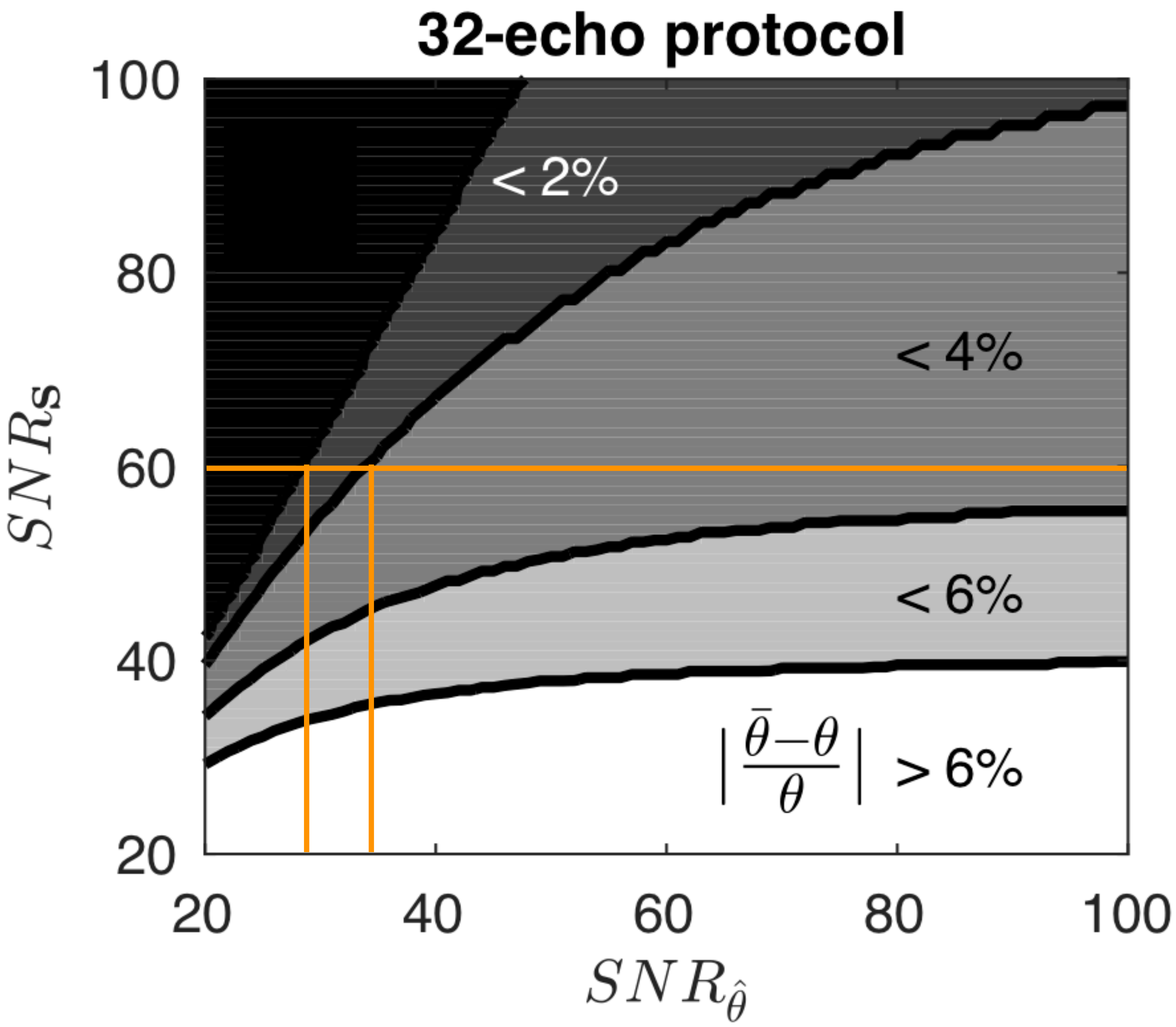

Summary

- Nuisance parameters affect accuracy and precision of qMRI
- Propagation of error provides a relatively easy framework to compute these effects
  - can be extended to arbitrarily complex problems
- E.g., T_2 measurement: measuring flip angle may or may not reduce MSE(T_2), depending on the accuracy and precision of the flip angle measurements
- Need better characterization of the accuracy and precision of B_1 and B_0 mapping methods